

REMARKS/ARGUMENTS.

Claim 1 has been amended by claiming radiolabelled gallium metal complexes which are in a form suitable for use in PET or SPECT radiopharmaceutical imaging. Basis can be found at page 4 lines 14-18 of the specification.

1. CLAIM REJECTIONS: 35 USC §103.

Claims 1-3, 5 and 8-15 stand rejected as being obvious over Griffiths (WO 03/059397) in view of Yngve [Int.Diss.Abs., 62 (2001)], Bottcher (US 5,439,863) and Lidstrom [Tet.Lett., 57, 9225-9283 (2001)] and in further view of Maier-Borst (GB 2056471 A) and Wheaton [Industr.Eng.Chem., 43, 1088-1093 (1951)] as stated in the Office Action mailed 22 February 2010.

The Examiner argues that Bottcher teaches that a “high energy input” accelerates the formation of neutral transition metal complexes. The Examiner also suggests that Bottcher teaches that an advantage of the process described is “ease of separation of the formed complexes”. Applicants point out that Bottcher teaches repeatedly that the separation of the metal complexes is by precipitation and/or crystallization:

- (i) Column 2 lines 47-68;
- (ii) Column 3 lines 23-37;
- (iii) Column 3 lines 45-49;
- (iv) Column 3 line 64 – column 4 line 2;
- (v) Column 5 line 63 – column 6 line 2;

- (vi) Column 6 lines 3-8;
- (vii) Column 6 lines 16-22;
- (viii) Examples 1 to 4;
- (ix) Claim 1 which refers to “recovering the product in fine crystalline form”

Thus, the teaching of Bottcher is very clear, that the advantages taught therein are linked to precipitation/crystallization of the desired metal complex from the reaction mixture.

The “continuous conversion” referred to by the Examiner as an advantage of Bottcher, requires precipitation (Bottcher Column 3 lines 45-49).

Applicants stress that the method of present claim 1 does not have such a crystallization/precipitation step. Line 2 of claim 1 has the feature “in a suitable solvent” – thus the reaction is carried out in solution. The radioactive gallium complex would not precipitate, since they are required to be in a form suitable for radiopharmaceutical use. Radiopharmaceuticals are typically administered by intravenous injection, and hence must be in solution and particle-free to satisfy patient safety criteria. The person skilled in the art of radiopharmaceuticals would know that fact as common general knowledge. The person skilled in the art could therefore have no motivation to apply Bottcher to the method of revised claim 1, since Bottcher teaches unequivocally that precipitation/crystallization is an essential feature of the process therein. In fact, Bottcher teaches away from the present claims by teaching towards such a precipitation/crystallization process.

In addition, as argued at length previously, the person skilled in the art would know that radiopharmaceuticals are never prepared on a kilogramme scale. The Examiner has responded that the present claim does not recite the scale/concentration. Applicants respectfully remind the Examiner that the claim is directed to the person skilled in the art. Revised claim 1 refers to radiopharmaceuticals, and hence the claim must be construed in that context. Applicants respectfully point out that it is not necessary to specify such scale/concentration details, since they are implicit when the term 'radiopharmaceutical' is an essential feature. Thus, revised claim 1 refers to "radiolabelled gallium complex in a form suitable for use in PET/SPECT radiopharmaceutical imaging". The person skilled in the art would know from the use of such a phrase that (i) the kilogramme scale is not suitable for radioactive/radiopharmaceutical preparations; (ii) radiopharmaceuticals are rarely, if ever, isolated in solid form since the concentrations employed are much too low, and solid radiopharmaceuticals would likely suffer from severe radiolysis (i.e. radiolytic instability) problems due to the high level of concentration of radioactive emissions.

The alleged motivation to combine Bottcher with Griffiths/Yngve, therefore does not exist, and the inventive step rejection based on Bottcher should be withdrawn.

The Examiner also relies on Lidstrom. The Examiner also states (paragraph 16) that the Shaabani reference was not found in PAIR. Please find attached the Shaabani reference. Lidstrom is now stated in the Office Action mailed 06/28/1010 to be relied on simply for a general teaching on the increasing use of microwave technology in inorganic chemistry and organic synthesis (paragraphs 17 and 22 of the Office Action).

Applicants point out that the present Office Action maintains the same objection of that mailed 02/22/2010. The Office Action mailed 02/22/2010 (at paragraph 12) used Lidstrom more specifically, referring to the entry therein on organometallic reactions (Lidstrom p.9267, last entry). Applicants respectfully submit that the Examiner cannot now arbitrarily choose to ignore the previously-cited, specific teaching of Lidstrom on the most closely-related technology in favor of only the more general teaching therein. Suitable reasoning or justification is respectfully requested as to why the person skilled in art would choose to ignore the clear teaching of Lidstrom – otherwise the Examiner's position, according to Applicants point-of-view, represents a clear application of hindsight.

Further, Applicants stress that Lidstrom is a comprehensive review, citing 603 references - yet only one reference to organometallic reactions is cited. That reference (#521; Shaabani) is to a solvent-free, metal template synthesis. Hence, the person skilled in the art reading Lidstrom at the priority date of the present invention could have no motivation to combine Lidstrom and Griffiths/Yngve, since the single organometallic reaction taught by Lidstrom is completely different in nature to that of Griffiths/Yngve. Hence, the only teaching of Lidstrom on organometallic reactions is that relied on previously by the Examiner. That same teaching is what Lidstrom provided to the person skilled in the art at the priority date of the present invention. Since present claim 1 refers to organometallic chemistry, the Examiner must justify why the person skilled in the art would be motivated to ignore that clear teaching. Applicants stress that Lidstrom provides only one instance of an organometallic metal complexation reaction using microwave had been reported in the

literature, and that used solvent-free concentrations. In addition, as argued previously, that one reference (Shaabani *et al.*) refers to a metal template synthesis.

The inventive step rejection based on the combination of Lidstrom and Griffiths/Yngve should therefore also be withdrawn.

Since only Lidstrom and Bottcher provide the microwave heating feature of revised claim 1, the rejection is believed to have been overcome in its entirety. The rejection of claims 1-3, 5 and 8-15 should therefore be withdrawn.

2. DOUBLE PATENTING.

Claims 1-3, 5 and 7 and 15 are provisionally rejected in this regard over corresponding application USSN 10/552206.

Claims 1-3, 5 and 7 and 15 provisionally rejected in this regard over corresponding application USSN 111/358681.

Applicants will file a suitable terminal disclaimer when this application is deemed allowable.

Appl. No. 10/552,134
Amdt. Dated: October 28, 2010
Reply to Office Action of June 28, 2010

CONCLUSION

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

/Craig Bohlken/

Craig Bohlken
Reg. No. 52,628

GE Healthcare, Inc.
101 Carnegie Center
Princeton, NJ 08540
Phone (609) 514-6530

EMPResponse to Office ActionPHNPH0334 (10-28-2010).doc